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VASCULAR DISEASE

ANDROGENS STIMULATE HUMAN ENDOTHELIAL PROGENITOR CELL FUNCTION AND HUMAN CORONARY COLLATERALIZATION

ACC Poster Contributions
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Background: The role of androgens in cardiovascular diseases remains controversial. Recent studies have described an inverse relationship between androgen levels and cardiovascular mortality in men. Endothelial progenitor cells (EPCs) are important for angiogenesis, and it has been linked to cardiovascular outcomes. We hypothesize that androgen plays a role in enhancing human male angiogenesis through EPC.

Methods: EPCs were isolated from healthy young male donors (n=12), and treated with dihydrotestosterone (DHT, 4-400nM), ±androgen receptor (AR) antagonist, hydroxyflutamide, ±oestrogen receptor antagonist, ICI182780, and their functions were assessed. To assess angiogenesis in vivo, DHT-treated Early- and Late- EPCs were xenotransplanted into BalbC nu/nu male mice following hindlimb ischemia. Male patients (n=14) having elective percutaneous coronary intervention were recruited to assess coronary collateralization, including collateral flow index (CFI).

Results: DHT induced a dose-dependent increase in ulex-lectin+/AcLDLcells ($P<0.05$), in Early-EPC migration ($P<0.05$) and tubulogenesis ($P<0.001$). Hydroxyflutamide completely abolished DHT-mediated effects on Early-EPC number and migration; ICI182780 had no effect. Similar findings were also observed for Late-EPCs (all $P<0.05$). Mice xenotransplanted with Early-EPCs treated with 400nM DHT showed better recovery using Doppler imaging at Day14 ($P<0.05$) and Day21 ($P<0.05$) post-surgery than control mice, and mice xenotransplanted with DHT treated Late-EPC showed even more robust response ($P<0.05$ at Day 14 and 21). In the human coronary collateral study, free testosterone levels correlated significantly with CFI ($r=0.786$, $P=0.021$). No relationship was established between oestradiol and CFI. Free testosterone levels correlated negatively with Early-EPC ($r=-0.78$, $P=0.036$), but positively with Late-EPC ($r=0.9$, $P=0.037$) number.

Conclusion: This study provides in vitro, in vivo, and clinical evidence of pro-angiogenic effects of androgen. These effects are likely to be mediated through AR on Late-EPCs. This study highlights the potential benefit of androgen replacement for men's cardiovascular health.